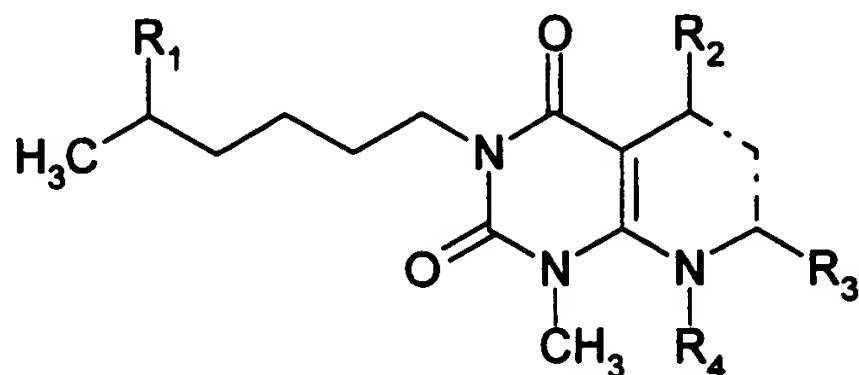
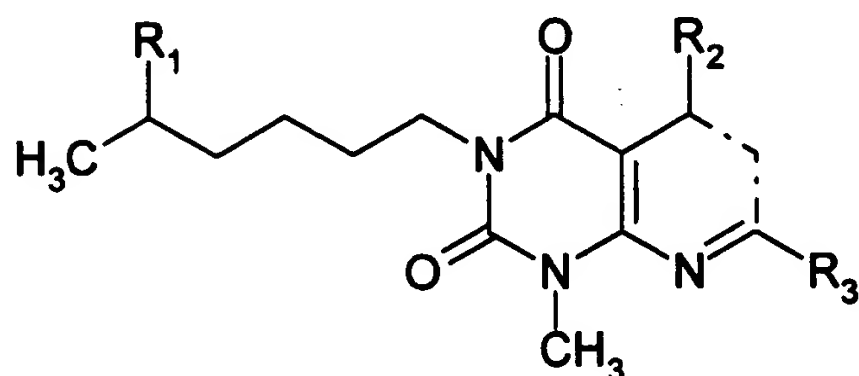


APPENDIX A

1. A therapeutic compound, including resolved enantiomers, diastereomers, tautomers, salts and solvates thereof, having one of the following formulae:



or



wherein:

R₁ is selected from a member of the group consisting of hydrogen, hydroxyl, methoxyl, acylamino group, cyano group, sulfo, sulfinyl, sulfhydryl (mercapto), sulfeno, sulfanilyl, sulfamyl, sulfamino, and phosphino, phosphinyl, phospho, phosphono and -NR_aR_b, wherein each of R_a and R_b may be the same or different and each is selected from the group consisting of hydrogen and optionally substituted: C₍₁₋₂₀₎alkyl, C₍₃₋₁₂₎cycloalkyl, C₍₂₋₂₀₎alkenyl, C₍₃₋₁₂₎cycloalkenyl, C₍₂₋₂₀₎alkynyl, aryl, heteroaryl, and heterocyclic group;

R₂ and R₃ are independently selected from a member of the group consisting of halo, oxo, C₍₁₋₂₀₎alkyl, C₍₁₋₂₀₎hydroxyalkyl, C₍₁₋₂₀₎thioalkyl, C₍₁₋₂₀₎alkylthio, C₍₁₋₂₀₎alkylaminoalkyl, C₍₁₋₂₀₎aminoalkyl, C₍₁₋₂₀₎aminoalkoxyalkenyl, C₍₁₋₂₀₎aminoalkoxyalkynyl, C₍₁₋₂₀₎diaminoalkyl, C₍₁₋₂₀₎triaminoalkyl, C₍₁₋₂₀₎tetraaminoalkyl, C₍₁₋₂₀₎alkylamido, C₍₁₋₂₀₎alkylamidoalkyl, C₍₁₋₂₀₎amidoalkyl, C₍₁₋₂₀₎acetamidoalkyl, C₍₂₋₂₀₎alkenyl, C₍₂₋₂₀₎alkynyl, C₍₁₋₂₀₎alkoxyl, C₍₁₋₂₀₎alkoxyalkyl, C₍₁₋₂₀₎dialkoxyalkyl, and -NR_aR_b; and

R₄ may be hydrogen or an optionally substituted member of the group consisting of C₍₁₋₂₀₎alkyl, C₍₃₋₁₂₎cycloalkyl, C₍₂₋₂₀₎alkenyl, C₍₃₋₁₂₎cycloalkenyl, C₍₂₋₂₀₎alkynyl, aryl, heteroaryl, and heterocyclic group.

2. The therapeutic compound of claim 1, wherein R₂ and R₃ are independently selected from a member of the group consisting of hydrogen, halo, thio, oxo, C₍₁₋₁₀₎alkyl, C₍₁₋₁₀₎hydroxyalkyl, C₍₁₋₁₀₎thioalkyl, C₍₁₋₁₀₎alkylthio, C₍₁₋₁₀₎alkylamino, C₍₁₋₁₀₎alkylaminoalkyl, C₍₁₋₁₀₎aminoalkyl, C₍₁₋₁₀₎aminoalkoxyalkenyl, C₍₁₋₁₀₎aminoalkoxyalkynyl, C₍₁₋₁₀₎diaminoalkyl, C₍₁₋₁₀₎triaminoalkyl, C₍₁₋₁₀₎tetraaminoalkyl, C₍₁₋₁₀₎aminotrialkoxyamino, C₍₁₋₁₀₎alkylamido, C₍₁₋₁₀₎alkylamidoalkyl, C₍₁₋₁₀₎amidoalkyl, C₍₁₋₁₀₎acetamidoalkyl, C₍₂₋₁₀₎alkenyl, C₍₂₋₁₀₎alkynyl, C₍₁₋₁₀₎alkoxyl, C₍₁₋₁₀₎alkoxyalkyl, and C₍₁₋₁₀₎dialkoxyalkyl.

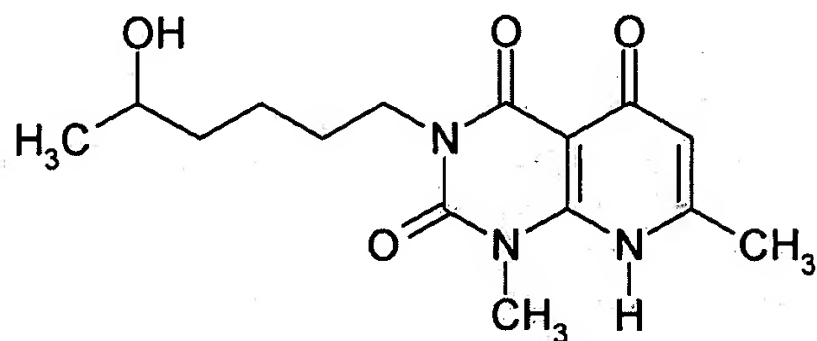
4. (Amended) The therapeutic compound of claim 37, wherein each of R₂ and R₃ is substituted with one or more members of the group consisting of hydroxyl, methyl, carboxyl, furyl, furfuryl, biotinyl, phenyl, naphthyl, amino group, amido group, carbamoyl group, cyano group, sulfo, sulfonyl, sulfinyl, sulfhydryl, sulfeno, sulfanilyl, sulfamyl, sulfamino, phosphino, phosphinyl, phospho, phosphono, N-OH, -Si(CH₃)₃, C₍₁₋₃₎alkyl, C₍₁₋₃₎hydroxyalkyl, C₍₁₋₃₎thioalkyl, C₍₁₋₃₎alkylamino, benzyl dihydrocinnamoyl group, benzoyl dihydrocinnamido group, optionally substituted heterocyclic group and optionally substituted carbocyclic group.

5. The therapeutic compound of claim 4, wherein the heterocyclic group or carbocyclic group is substituted with one or more members of the group consisting of halo, hydroxyl, nitro, SO₂NH₂, C₍₁₋₆₎alkyl, C₍₁₋₆₎haloalkyl, C₍₁₋₆₎alkoxyl, C₍₁₋₁₁₎alkoxyalkyl, C₍₁₋₆₎alkylamino, and C₍₁₋₆₎aminoalkyl.

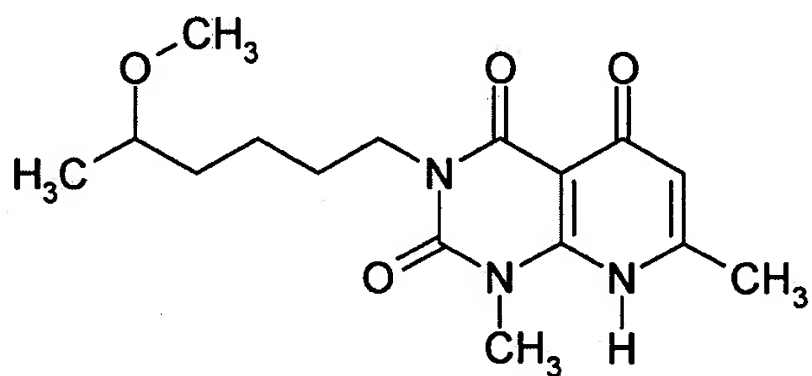
6. The therapeutic compound of claim 4, wherein the heterocyclic group is a member selected from the group consisting of acridinyl, aziridinyl, azocinyl, azepinyl, benzimidazolyl, benzodioxolanyl, benzofuranyl, benzothiophenyl, carbazole, 4a H-carbazole, chromanyl, chromenyl, cinnolinyl, decahydroquinolinyl, dioxoindolyl, furazanyl, furyl, furfuryl, imidazolidinyl, imidazolynyl, imidazolyl, 1H-indazolyl, indolenyl, indolynyl, indolizynyl, indolyl, 3H-indolyl, isobenzofuranyl, isochromanyl, isoindolynyl, isoindolyl, isoquinolinyl, isothiazolyl, isoxazolyl, morpholynyl, naphthyridinyl, octahydro-isoquinolinyl, oxazolidinyl, oxazolyl, oxiranyl, perimidinyl, phenanthridinyl, phenanthrolinyl, phenarsazinyl, phenazinyl, phenothiazinyl, phenoxathiinyl, phenoxazinyl, phthalazinyl, piperazinyl, piperidinyl, 4-pipendonyl, piperidyl, pteridinyl, purinyl, pyranyl, pyrazinyl, pyrazolidinyl, pyrazolynyl, pyrazolyl, pyridazinyl, pyndinyl, pyridyl, pyndyl, pyrimidinyl, pyrrolidinyl, 2-pyrrolidonyl, pyrrolonyl, pyrrolyl, 2H-pyrrolyl, quinazolynyl, 4H-quinolizynyl, quinolynyl, quinoxalynyl, quinuclidinyl, β -carbolynyl, tetrahydrofuranyl, tetrahydroisoquinolinyl, tetrahydroquinolinyl, tetrazolyl, 6H-1,2,5-thiadiazinyl, 2H-,6H-1,5,2-dithiazinyl, thianthrenyl, thiazolyl, thienyl, thiophenyl, triazinyl, xanthenyl and xanthinyl.

7. The therapeutic compound of claim 4, wherein the carbocyclic group is a member selected from the group consisting of adamantyl, anthracenyl, benzamidyl, benzyl, bicyclo[2.2.1]heptanyl, bicyclo[2.2.1]hexanyl, bicyclo[2.2.2]octanyl, bicyclo[3.2.0]heptanyl, bicyclo[4.3.0]nonanyl, bicyclo[4.4.0]decanyl, biphenyl, biscyclooctyl, cyclobutyl, cyclobutenyl, cycloheptyl, cycloheptenyl, cyclohexanedionyl, cyclohexenyl, cyclohexyl, cyclooctanyl, cyclopentadienyl, cyclopentanedionyl, cyclopentenyl, cyclopentyl, cyclopropyl, decalynyl, 1,2-diphenylethanyl, indanyl, 1-indanonyl, indenyl, naphthyl, naphthalenyl, phenyl, resorcinolyl, stilbenyl, tetrahydronaphthyl, tetralinyl, tetralonyl, and tricyclododecanyl.

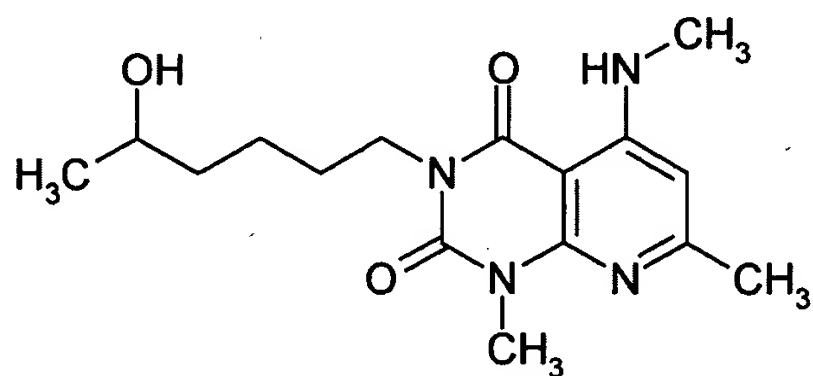
8. A compound, including resolved enantiomers, diastereomers, tautomers, salts and solvates thereof, having the formula:



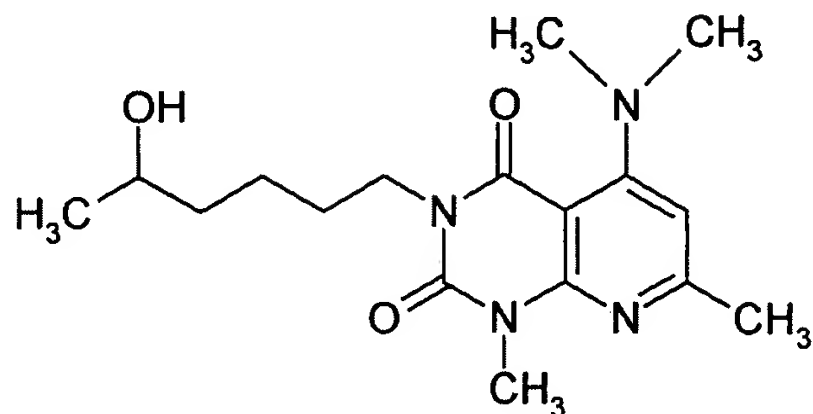
9. A compound, including resolved enantiomers, diastereomers, tautomers, salts and solvates thereof, having the formula:



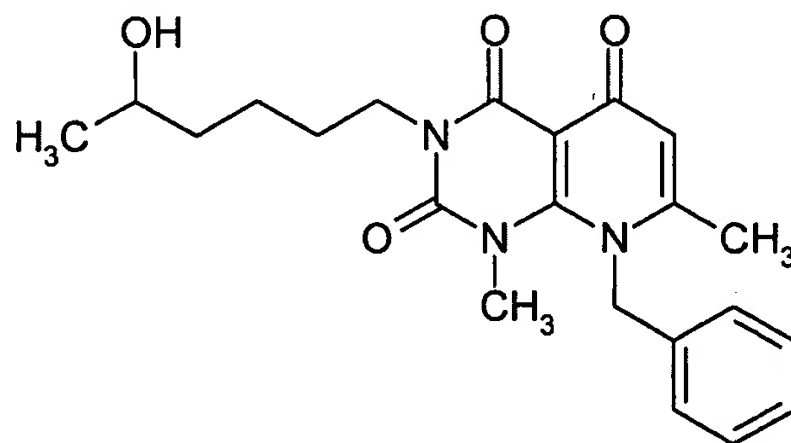
10. A compound, including resolved enantiomers, diastereomers, tautomers, salts and solvates thereof, having the formula:



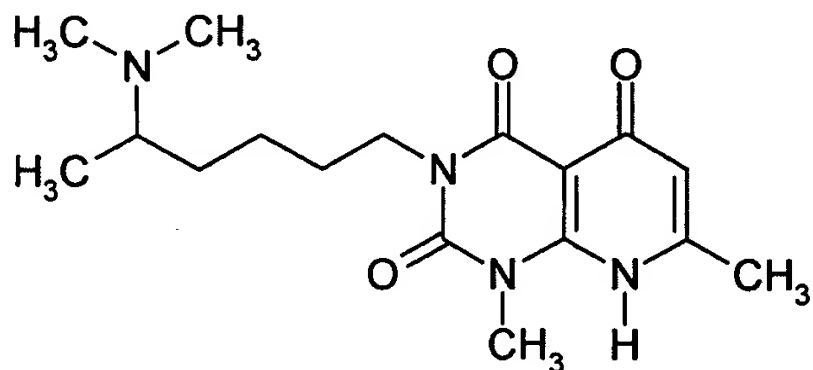
11. A compound, including resolved enantiomers, diastereomers, tautomers, salts and solvates thereof, having the formula:



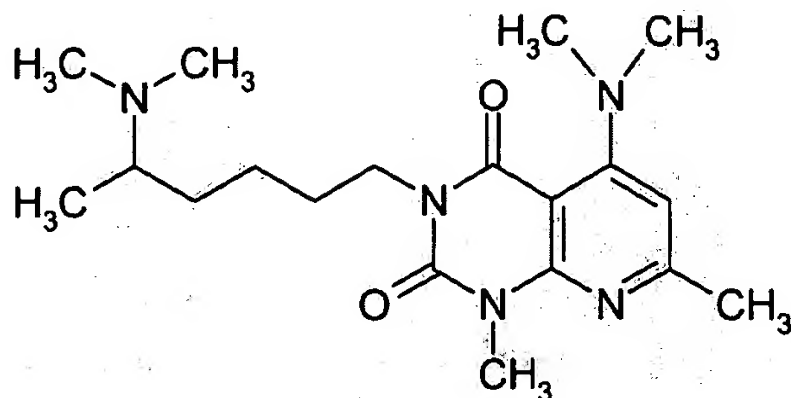
12. A compound, including resolved enantiomers, diastereomers, tautomers, salts and solvates thereof, having the formula:



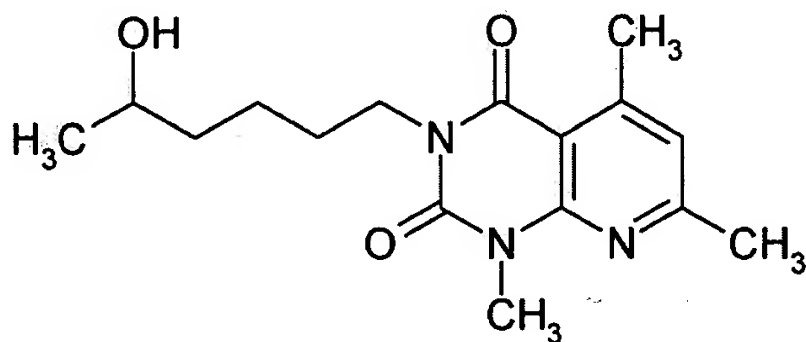
13. A compound, including resolved enantiomers, diastereomers, tautomers, salts and solvates thereof, having the formula:



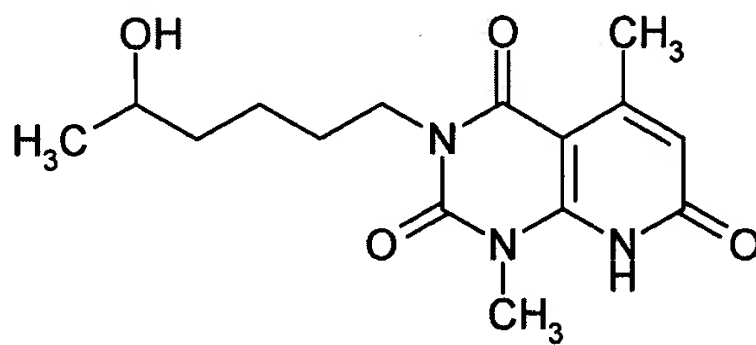
14. A compound, including resolved enantiomers, diastereomers, tautomers, salts and solvates thereof, having the formula:



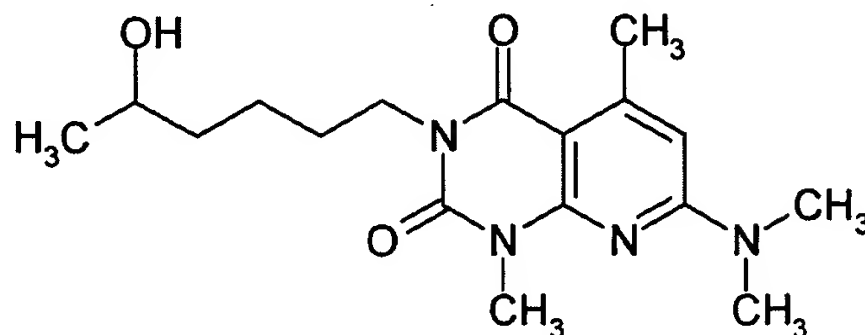
15. A compound, including resolved enantiomers, diastereomers, tautomers, salts and solvates thereof, having the formula:



16. A compound, including resolved enantiomers, diastereomers, tautomers, salts and solvates thereof, having the formula:



17. A compound, including resolved enantiomers, diastereomers, tautomers, salts and solvates thereof, having the formula:



18. A pharmaceutical composition comprising the compound of claim 1 in admixture with a pharmaceutically acceptable carrier, adjuvant or vehicle.

19. A method for inhibiting an activity mediated by a cytokine, the method comprising:

- (a) contacting cytokine responsive cells with a compound as defined in claim 1; and
- (b) determining that the cellular process or activity mediated by the cytokine is inhibited.

20. The method of claim 19, wherein step (a) is carried out *in vitro*.

21. The method of claim 19, wherein said cellular process is the differentiation of naïve T cells into Th1 or T1 cells.

22. The method of claim 19, wherein said cellular process is the differentiation of naïve T cells into Th2 or T2 cells.

23. The method of claim 19, wherein said activity is the secretion of proinflammatory cytokines.

24. The method of claim 19, wherein said activity is the secretion of anti-inflammatory cytokines.

25. The method of claim 19, wherein said activity is the secretion of a cytokine selected from the group consisting of tumor necrosis factor, colony stimulating factor, interferon, IL-1, IL-2, IL-3, IL-4, IL-5, IL-6, IL-7, IL-8, IL-9, IL-10, IL-11, IL-12, IL-13, IL-14, IL-15, transforming growth factor, oncostatin M, leukemia inhibiting factor, and platelet activating factor.

26. The method of claim 25, wherein said cytokine is IL-12.

27. The method of claim 25, wherein said cytokine is IL-4.

28. A method for treating a T1 cell-mediated inflammatory response in a mammal in need of such treatment, the method comprising administering to the mammal a therapeutically effective amount of the compound of claim 1, wherein said compound is capable of inhibiting an IL-12 mediated cellular process or activity, thereby inhibiting the inflammatory response.

29. The method of claim 28, wherein the inflammatory response is associated with a disease or condition selected from the group consisting of chronic inflammatory disease, chronic intestinal inflammation, arthritis, psoriasis, asthma and autoimmune disorders.

30. The method of claim 28, wherein said autoimmune disorder is selected from Type-1 IDDM, multiple sclerosis, rheumatoid arthritis, uveitis, inflammatory bowel disease, lupus disorders, and acute and chronic graft-versus-host disease.

31. The method of claim 28, wherein said mammal is a human.

32. A method for treating a T2 cell-mediated anti-inflammatory response in a mammal in need of such treatment, the method comprising administering to the mammal a therapeutically effective amount of the compound of claim I, wherein said compound is capable of inhibiting an IL-4 mediated cellular process or activity, thereby inhibiting antiinflammatory response.

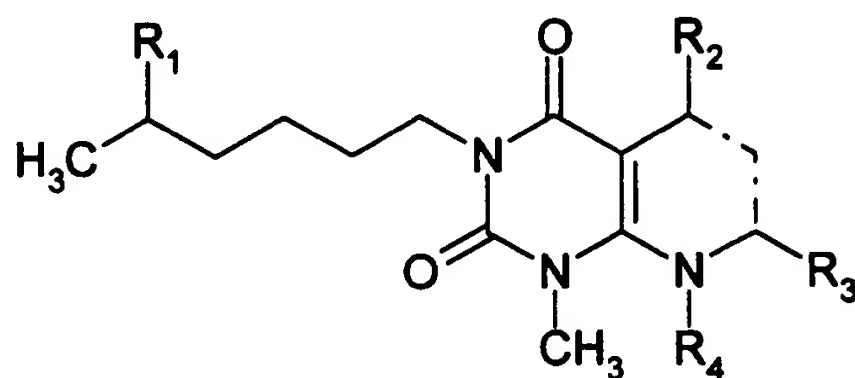
33. The method of claim 32, wherein the anti-inflammatory response is associated with a disease or condition selected from the group consisting of asthma, atopic dermatitis, hay fever, eczema, urticaria and food allergy.

34. The method of claim 33, wherein said disease is asthma.

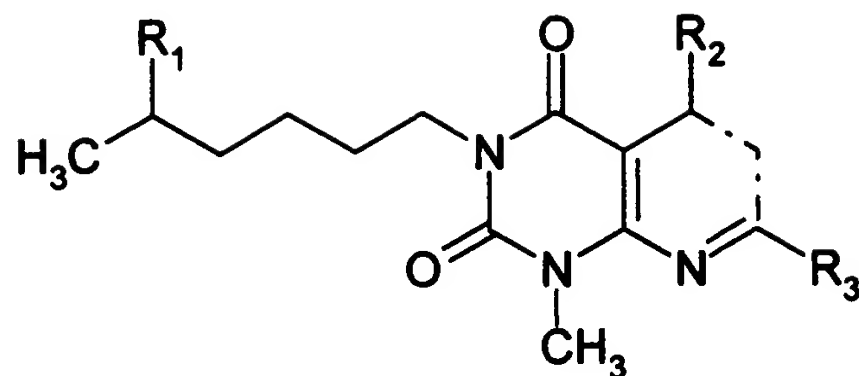
35. The method of claim 32, wherein said mammal is a human.

36. A method for treating NIDDM comprising a step of administering to a subject in need of such treatment a therapeutically effective amount of a compound of claim 1.

37. A therapeutic compound, including resolved enantiomers, diastereomers, tautomers, salts and solvates thereof, having one of the following formulae:



or



wherein:

R₁ is selected from a member of the group consisting of hydrogen, hydroxyl, methoxyl, acylamino group, cyano group, sulfo, sulfonyl, sulfinyl, sulfhydryl (mercapto), sulfeno, sulfanilyl, sulfamyl, sulfamino, phosphino, phosphinyl, phospho, phosphono and -NR_aR_b, wherein each of R_a and R_b may be the same or different and each is selected from the group consisting of hydrogen and optionally substituted: C₍₁₋₂₀₎alkyl, C₍₃₋₁₂₎cycloalkyl, C₍₂₋₂₀₎alkenyl, C₍₃₋₁₂₎cycloalkenyl, C₍₂₋₂₀₎alkynyl, aryl, heteroaryl, and heterocyclic group;

R₂ and R₃ are independently selected from a unsubstituted or substituted member of the group consisting of methyl, ethyl, oxo, isopropyl, n-propyl, isobutyl, n-butyl, t-butyl, 2-hydroxyethyl, 3-hydroxypropyl, 3-hydroxy-n-butyl, 2-methoxyethyl, 4-methoxy-n-butyl, 5-hydroxyhexyl, 2-bromopropyl, 3-dimethylaminobutyl, 4-chloropentyl, methylamino, aminomethyl, and methylphenyl; and

R₄ may be hydrogen or an optionally substituted member of the group consisting of C₍₁₋₂₀₎alkyl, C₍₃₋₁₂₎cycloalkyl, C₍₂₋₂₀₎alkenyl, C₍₃₋₁₂₎cycloalkenyl, C₍₂₋₂₀₎alkynyl, aryl, heteroaryl, and heterocyclic group.